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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/575,217	05/07/2007	Christof Niehrs	025953-001	6923

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EXAMINER	
MARVICH, MARIA	

ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/575,217	NIEHRS ET AL.	
	Examiner	Art Unit	
	MARIA MARVICH	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 February 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9,11-24,27,28 and 32-34* is/are pending in the application.

4a) Of the above claim(s) *9 and 11-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-24,27,28 and 32-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 September 2010* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to an amendment filed 2/22/01. Claims 9, 11-24, 27, 28 and 32-34 are pending.

This application contains claims drawn 9, 11-20 drawn to an invention nonelected with traverse in the reply filed on 12/18/09 A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01. Therefore, claims 21-24, 27, 28 and 32-34 are under examination.

The amendment is sufficient to overcome the previous objections, the rejection under 35 USC 112, second and 112 first paragraph. As well, applicant arguments are sufficient to overcome the rejection as anticipated by or obvious over Warner et al.

Claim Objections

Claims 21 and 30 are objected to because of the following informalities: **These are new claim objections.** Claim 21 requires amendment of several informalities to provide clarity. First, in line 2 the preamble should read, --wherein the binding partner affects Wnt signaling--. As well, in step b) amendment to --binding of the compound to the Futrin 2 has occurred to form a Futrin 2/binding partner--. The first amendment provides clearer antecedent basis while the second a more direct relationship.

For direct antecedent basis, claim 23 should be amended to recite, --determining if the altered activity is inhibition of the Wnt signaling--.

And similarly in claim 28 amendment to --wherein the step of assaying comprises determining if the binding partner exhibits--.

In claim 32, an article is required prior to "Futrin 2" in line 1 and 2. In this case, the article should be --the--.

As well, the recitation of "a Wnt inducible luciferase reporter assay in a cellular system expressing Futrin 2 polypeptide" does not provide clear steps for a person to measure the activity of Futrin 2. It appears as if Furtin 2 has activated the Wnt signaling pathway, the luciferase assay will detect signaling Wnt. Furthermore, it appears as if the Furtin 2, the compound and Wnt are in an in vivo cellular system. For clarity, it is recommended that the claim be amended to recite, --wherein the contacting is in vivo in a cellular system expressing Futrin 2 polypeptide and comprising a vector comprising a reporter gene under control of a Wnt-inducible promoter and the assaying the Futrin activity comprises measuring luciferase activity--.

Appropriate correction is required.

Applicant is advised that should claim 23 be found allowable, claim 33 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Both claims have the same scope in that the assay is to measure if the Wnt signaling activity of the Furtin 2 polypeptide is inhibited.

Claim Rejections - 35 USC § 102 or 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 21-24, 27, 28, 33 and 34 are rejected under as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Tang et al WO 01/77169. **This rejection is maintained for reasons of record in the office action mailed 11/22/10.**

The instant application teaches that Futrin 2 was previously identified

> [0012] During the experiments resulting in the present invention four genes, futrin 1, 2, 3 and 4, could be identified the products of which are modulators of the Wnt pathway. Futrin 2 was previously identified as hPWTSR (Chen et al., 29 (2002), Mol. Biol. Rep. 287-292), a protein of before unknown role or function, expressed in numerous cell types. Further, human Futrin 1, 2, 3, and 4 were described as Stem Cell Growth Factor-Like Polypeptides, which are able to promote proliferation of hematopoietic stem cells (WO-A-01/77169; WO-A-01/07611).

Tang et al teaches use of the peptides in methods of determining binding partners (see e.g. page 88, lines 8-20). This peptide would inherently have the sequence of SEQ ID NO:26. The test compound can be an antibody (see e.g. page 133, line 5-10, page 134, line 11-23,. Section 5.17). Such immunological assays and binding assays cited traditionally include means to determine amount of antibody or compound bound (see e.g. page 151, line 10-29, i.e. radio-immunoassays). As well as binding, affect of activity of the peptide is analyzed (see e.g. page 109, line 5-22, 12-18, section 5.9.14 and 5.18) as well as level of expression (see e.g. section 5.18). The compound can be tagged (see e.g. page 109, line 19-24, page 134, line 11). It is noted that binding assays typically are drawn to addition of a known amount of peptide with a

test compound followed by a measure of amount of bound and unbound peptide. Hence, a practitioner would following classic methods of binding assays determine the level of protein before and after binding. The compounds are used for treatment such as cancer (see e.g. 5.9.16).

As to claim 34, the instant specification identifies Futrin 2 as the same protein in Tang et al and hence it would be explicit that the sequences are the same.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 21-24, 27, 28, 33 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tang et al WO 01/77169 in view of Vernet et al (US 6,653,448; see entire document).

Applicants claim a method of identifying a binding partner for a Futrin 2 polypeptide that affects or inhibits Wnt signaling of the Futrin 2.

The teachings of Tang et al are as above, however, Tang et al do not teach that the signaling pathway is monitored using a luciferase reporter assay.

Vernet et al teaches that Wnt activity includes proliferation of hematopoietic cells (see col 57, line 17-48). The activity of Wnt is monitored by using a luciferase reporter assay (see e.g. bridging ¶ col 41-42).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to assay for modulation of downstream Futrin 2 events such as stem cell proliferation by assaying signaling pathways related thereto as taught by Tang et al by using a reporter construct that reports on signaling pathways related to stem cell proliferation as taught by Vernet et al because Tang et al teach that it is within the ordinary skill of the art to inhibit Futrin 2 and to do so will affect downstream signaling events and because Vernet et al and Tang et al teach that stem cell proliferation is the result of Futrin 2 and Wnt signaling respectively and because Vernet et al teach that it is within the ordinary skill of the art to use a Wnt responsive luciferase construct to assay signaling pathways. One would have been motivated to do so in order to receive the expected benefit of ease of assaying intracellular events. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

In KSR International Co. v. Teleflex Inc., 82 USPQ2d 1385 (U.S. 2007), the Supreme Court particularly emphasized "the need for caution in granting a patent based on a combination of elements found in the prior art," (Id. At 1395) and discussed circumstances in which a patent might be determined to be obvious. Importantly, the Supreme Court reaffirmed principles based on its precedent that obviousness in part is predicated on use of particular known techniques that are recognized as part of the ordinary capabilities of one skilled in the art. In the instant case, it is accepted that use of reporter constructs is designed to improve detecting intracellular events with predictable results. As well, it is within the ordinary skill of the art to use available methodologies to isolate a variety of sequences comprising any of a number of spacer sequences

and one would have been motivated to do so in order as the ability to modify sequences by applying conventional methodologies. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Response to amendment

Applicants argue that the method of the instant claims is not taught by Tan or Warren and any comment about inherency of the method is pure speculation. Applicants' arguments have been considered but are not persuasive for the following reasons. To examine the anticipation of the teachings, it is important to understand what steps are required. The claimed invention comprises

a) contacting Futrin 2 with a compound

b) determining IF a complex forms between the two

c) assaying the complex to determine if Wnt signaling is affected.

As a first point, there is no requirement that the complex be formed. But in the instance it is formed, the method requires that the complex be assayed for affect on Wnt signaling.

Tang et al teach these steps as set forth below.

a) contacting Futrin 2 with a compound

"the proteins provided by the present invention can similarly be used" " to isolate correlative receptors or ligands Where the protein binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the protein can be used to identify the other protein with which binding occurs or to identify inhibitors of the binding interaction.

Proteins involved in these binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction." (page 88)

b) determining formation of a complex,

> "In general, therefore such methods for identifying compounds that bind to a polynucleotide of the invention can comprise contacting a compound with a polynucleotide of the invention for a time sufficient to form a polynucleotide/compound complex, and detecting the complex, so that if a polynucleotide/compound complex is detected, a compound that binds to a polynucleotide of the invention is identified." (page 153)

c) The compounds are assayed for modulation of the peptide activity.

> "Sources for test compounds that may be screened for ability to bind to or modulate (i.e. increase or decrease) the activity of polypeptides of the invention include (1) inorganic or organic chemical libraries, (2) natural product libraries, and (3) combinatorial libraries comprised of either random or mimetic peptides, oligonucleotides or organic molecules" (page 109).
>
> "The role of downstream intracellular signaling molecules in the signaling cascade of the polypeptide of the invention can be determined" (page 111).

It appears as if the only difference between the two claims is explicit recitation that the Wnt signaling pathway is assessed to identify effects of a binding partner of Futrin 2. However, the effect of binding on downstream signaling is explicitly encompassed by Tang et al. Furthermore, Tang et al teach that Futrin 2 is involved in proliferation of hematopoietic stem cells (see page 86) which is recognized in the art as regulated by Wnt signaling.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARIA B. MARVICH whose telephone number is (571)272-0774. The examiner can normally be reached on M-F (7:00-4:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, PhD can be reached on (571)-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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